Remarks

Upon entry of the present amendments, claims 7-12, 21-28, 32-39, 43-44, 47-54 are pending in this application. Claims 1-6, 13-14, 16-18, 29-31, and 40-42 were previously canceled without prejudice. Claims 15, 19-20 and 45-46 are currently canceled without prejudice to Applicant's right to pursue the subject matter recited by them in one of more divisional, continuation, and/or continuation-in-part applications. Claims 49-54 are added, and claims 7-8, 26-27, 33, and 43 are amended for formal reasons. No new matter has been introduced. Applicant respectfully submits that the pending claims are allowable for at least the following reasons.

First, Applicant wishes to thank Examiner Jones for the courtesy he extended to Hoon Choi, an attorney for Applicant, during a telephone conversation on February 9, 2005. During that conversation, the Examiner confirmed that the rejection raised in item 19 of the Office Action was unintentional. Other rejections are addressed below.

A. The Rejection under 35 U.S.C. § 112 Should be Withdrawn

a. Enablement

In items 11-12 of the Office Action, claims 7-12, 21-28, 32-39, 43-44, and 47-48 are rejected as allegedly not enabled. In particular, it is alleged that the specification does not provide enablement for "inhibiting angiogenesis" and "treating angiogenesis dependent disease," based on the analysis of factors set forth in *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) ("*Wands* factors") Office Action, pages 7-13. Applicant respectfully traverses this rejection.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *U.S. v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988). The examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *Manual of Patent Examining Procedure* ("MPEP") § 2164.04 (citing *In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993)). Accordingly:

> A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must be taken as being in compliance with the enablement requirement* ... unless there is *a reason to doubt the objective truth*

> *of the statements* contained therein which must be relied on for enabling support
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> * * *
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> It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to *explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning* which is inconsistent with the contested statement.

Id. (emphases added).

Applicant respectfully submits that the pending claims are enabled because the specification "contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented." *Id.* For example, the specification teaches that angiogenesis can be inhibited, or an angiogenesis dependent disease can be treated, by using the compounds recited by claims 26 and 27. *See, e.g.*, the specification, page 13-16, and page 21, lines 26-30. It is also disclosed that these compounds can be commercially obtained, or prepared using standard procedures known in the art. *See*, the specification, page 21, lines 8-11. Dosages and routes of administration are disclosed, for example, on page 23, lines 18-33 of the specification. All that is required for those of ordinary skill in the art to practice the claimed invention is to administer the specified amount of the specified compound using the specified routes of administration. Therefore, it is clear that a sufficient guidance is provided in the specification so as to allow those of ordinary skill in the art to make and use the claimed invention.

In addition, Applicant respectfully submits that the Examiner's analysis of *Wands* factors does not provide a factual basis that supports the allegation that the pending claims are not enabled. For example, while it is alleged that the relative skill in the art is "high," and the unpredictability in pharmaceutical art is "high," no factual support for these allegations is provided in the Office Action.[1] Furthermore, in his analysis, the Examiner appears to believe that the pending claims only provide a functional recitation of "angiogenesis inhibiting compound." *See, e.g.*, the Office Action, page 10. This is not correct; all of the pending claims recite a structurally-defined genus of compounds. *See* claims 7, 26, and 27.

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[1] In fact, Applicant submits that these two allegations cut against each other.

Applicant also disagrees with the Examiner's allegation that the specification fails to provide sufficient guidance for those of ordinary skill in the art because "a disclosure should contain representative examples which provide reasonable assurance to one skilled in the art that the methods will fall within the scope of a claim and will possess the alleged activity." Office Action, page 12, citing *In re Riat*, 327 F.2d 685 (C.C.P.A. 1964) and *In re Barr*, 444 F.2d 588 (C.C.P.A. 1971). However, neither of these cases stand for the proposition that "reasonable assurance" that the methods "will possess the alleged activity" should be provided. In fact, these cases do not even concern enablement issues.

Thus, Applicant respectfully submits that the standard applied by the Examiner is legally incorrect: there is no requirement that those of ordinary skill in the art must be able to ascertain the claimed invention from the specification in order for the specification to be enabling. Instead, the standard is whether those of ordinary skill in the art would be able to make and use the claimed invention. *See Telectronics, Inc.*, 857 F.2d at 785.

Finally, Applicant respectfully submits that no undue experimentation is necessary to practice the claimed invention. Some factors that may --but need not[2]-- be considered in determining whether experimentation is undue include the quantity of experimentation necessary and the amount of direction or guidance provided. *In re Wands*, 858 F.2d at 737. In *Wands*, the Court of Appeals for the Federal Circuit held that claims directed to immunoassay methods were enabled even though in order to practice the claimed invention, one would have to screen "hybridomas to determine which ones secrete antibody with desired characteristics." This was because "[p]ractitioners of this art are prepared to screen negative hybridomas in order to find one that makes the desired antibody." *Id.* at 740.

As in *Wands*, the Examiner here is objecting to what is basically a screening step. Yet here, the screening is not nearly as complex, as the claimed invention is directed to the use of specific, readily obtainable compounds, for which routes of administration and amounts are set forth in the specification. Moreover, the determination by a physician as to whether a compound of this invention is effective in inhibiting angiogenesis and/or treating an angiogenesis dependent disease in a given patient is a type of determination that is always made by physicians for every pharmaceutical. Indeed, the determination is a routine one that every physician is prepared to make, and which requires little or no effort. Therefore,

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[2] *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.* , 927 F.2d 1200, 1230 (Fed. Cir. 1991), *cert. denied*, 502 U.S. 856 (1991) ("it is not necessary that a court review all the *Wands* factors to find a disclosure enabling. They are illustrative, not mandatory.").

Applicant respectfully submits that one reasonably skilled in the art could make or use the invention as claimed without undue experimentation.

In sum, Applicant respectfully submits that: (1) the specification provides sufficient information and guidance to those of ordinary skill in the art to make and use the claimed invention; (2) the Examiner did not provide any factual or legal basis to doubt that the claims are enabled; and (3) to the extent any experimentation is necessary, such experimentation is not undue. Therefore, Applicant respectfully requests that the rejection of the claims under 35 U.S.C. § 112, ¶ 1, be reconsidered and withdrawn.

b. Written Description

In item 13 of the Office Action, claims 27, 28, 37-39, and 48 are rejected for allegedly failing to comply with the written description requirement. In particular, it is alleged that the specification does not provide adequate written description of the phrase "treating angiogenesis dependent disease." Office Action, pages 13-14. Applicant respectfully traverses this rejection.

To satisfy the written description requirement, "a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention." *Manual of Patent Examining Procedure* ("MPEP"), § 2163.I. A description as filed is "presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. *Id.*, § 2163.04.

Here, Applicant submits that the specification provides sufficiently detailed disclosure for those of ordinary skill in the art to conclude the inventor had possession of the claimed invention. For example, the specification discloses that angiogenesis dependent diseases can be treated using methods of this invention. *See, e.g.*, the specification, page 21, lines 26-30. "Angiogenesis dependent diseases" are described in detail, for example, on page 2, line 27 - page 6, line 14 of the specification.

Clearly, those of ordinary skill in the art have no reason to conclude that the inventor did not have possession of the claimed invention, and no evidence to the contrary is provided in the Office Action. In fact, all that is provided in the Office Action is a conclusory allegation that the specification fails to provide adequate written description for the phrase "treating angiogenesis dependent disease." Office Action, page 13. Consequently, Applicant respectfully requests that the rejection of the claims under 35 U.S.C. § 112 be reconsidered and withdrawn.

In items 14-16, claims 15, 19, 20, 45, and 46 are also rejected as allegedly failing to complying with the written description requirement. Without addressing the substance of this rejection, Applicant respectfully points out that this rejection is obviated by the cancellation of those claims. Therefore, their rejection should also be reconsidered and withdrawn.

B. The Rejection of Claims 7-12, 21-28, 32-39, 43-44, and 47-48 Under 35 U.S.C. § 103(a) Should Be Withdrawn

In item 20 of the Office Action, claims 7-12, 21-28, 32-39, 43-44, and 47-48 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over WO 95/03807 by Billson *et al.* ("Billson"). In particular, it is alleged that these claims are obvious because Billson discloses the treatment of macular degeneration using anti-inflammatory agents it discloses, which can be optionally combined with thalidomide. Applicant respectfully traverses the rejection.

In response to Applicant's submission that Billson fails to teach the use of the claimed compounds, the Examiner appears to allege that the use of claimed compounds is disclosed in Billson because "claims 1 and 6-13 are composition claims, which are comprised of ...a functional recitation of an angiogenesis inhibitory compound and an anti-inflammatory compound." Office Action, paragraph 5. However, Applicant respectfully points out that claims 1 and 6 were previously canceled. And claim 7, the broadest composition claim, recites a genus of angiogenesis inhibitory compounds, which are not disclosed by Billson. Therefore, it is apparent that not all claim limitations are met by Billson. For this reason alone, Applicant respectfully submits that the rejection of the claims under 35 U.S.C. § 103 should be withdrawn.

Furthermore, as Applicant previously pointed out, the Examiner also has not provided the requisite support, based in the references of record, for his contention that the skilled artisan would have been motivated to utilize agents other than thalidomide (*e.g.*, its derivatives and analogues) in pharmaceutical compositions.

In response, the Examiner alleges that it is "surely within the level of the skilled artisan to utilize derivatives and analogues of a compound ... as long as the inherent properties of a given compound ... are not materially changed." Office Action, paragraph 7. As the Examiner recognizes, for those of ordinary skill in the art to use a particular derivative or analogue of a known compound, a determination as to whether that derivative or analogue retains substantially the same inherent properties of the original compound should be made for each possible derivative or analogue. Therefore, the Examiner apparently suggests that it

would have been obvious for those of ordinary skill in the art to try any number of derivatives or analogues of a known compound until they find a derivative or analogue that retains characteristics similar to those of original compound. This is flatly contrary to the well-settled legal principle that whether or not something may have been "obvious to try" cannot form the basis for a proper obviousness rejection. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1380 (Fed. Cir. 1986) (citing *Jones v. Hardy*, 727 F.2d 1524, 1530 (Fed. Cir. 1984) ("obvious to try" is improper consideration in adjudicating obviousness issue)). For at least this additional reason, Applicant respectfully submits that the rejection under 35 U.S.C. § 103 should be withdrawn.

Alternatively, in item 21 of the Office Action, claims 7-12, 21-28, 32-39, 43-44, and 47-48 are rejected as allegedly obvious over Billson, in view of U.S. Patent No. 5,348, 942 to Little, II *et al.* ("Little"). In particular, it is alleged that the claims are obvious because Billson discloses "methods of using ... an angiogenesis inhibitory compound (thalidomide) and an anti-inflammatory agent," and Little "teaches the skilled artisan that other ailments can be treated when angiogenesis is modulated," Office Action, item 9. Applicant respectfully traverses this rejection.

As discussed above, Billson does not disclose all of the limitations of the pending claims, and does not provide a motivation for those of ordinary skill in the art to arrive at the claimed invention. Little adds little to the substance of the rejection. As the Examiner recognizes, Little purportedly provides, at most, that "other ailments can be treated when angiogenesis is modulated." *Id.* From this, the Examiner contends that the "skilled artisan would have been motivated to treat other ailments that result from neovascularization or angiogenesis." *Id.*

But Little's alleged disclosure of disorders that may be treated by modulating angiogenesis would not have motivated those of ordinary skill in the art to combine Little with Billson. This is because Billson, while purportedly disclosing methods of treating macular degeneration using anti-inflammatory steroids, does not disclose that macular degeneration is a disorder modulated by angiogenesis. Furthermore, even if Billson and Little were combined, the combination still fails to disclose all of the limitations of the pending claims. Therefore, Applicant respectfully requests that the rejection of the claims under 35 U.S.C. § 103 be reconsidered and withdrawn.

C. The Rejection of Claim 9 under 35 U.S.C. § 103(a) Should be Withdrawn[3]

In the Office Action, claim 9 stands rejected over Billson, in view of Little. As an initial matter, and as noted above, Billson neither teaches nor suggests the compounds encompassed by claim 9. Little fails to rectify this error. For this reason alone, the pending rejection under 35 U.S.C. § 103 should be withdrawn.

The Examiner appears to contend that when the angiogenesis inhibitory composition is represented by the Applicant's compounds P, Q, R or S in claim 9, that one of skill in the art would recognize that these compounds would easily produce thalidomide via an internal cyclization reaction. In response to Applicant's request for support this allegation, the Examiner provides a copy of Solomons, *Organic Chemistry*, p.p 799-800, 802 and 806 (1984) ("Solomons"). Referring to the cyclic imide formation scheme disclosed in page 802 of Solomons, the Examiner alleges that compounds P, Q, R, or S would undergo similar reactions to provide thalidomide, and such "precursors" of a known compound would be obvious variants of the known compound. Office Action, item 6. Applicant respectfully disagrees.

The cyclic imide formation allegedly disclosed in Solomons involves a primary amine, while one of the hydrogens in amine groups present in compounds P, Q, R, and S is replaced with a bulky chemical moiety. As such, those of ordinary skill in the art would have concluded that the presence of such a bulky chemical moiety would sterically hinder the formation of cyclic imide, as opposed to the unsubstituted primary amine group purportedly disclosed in Solomons. Furthermore, Solomons purportedly discloses that the formation of cyclic imide occurs at an elevated temperature, with the required heating of the reaction to 150-160°C. Solomons, page 802. As such, even apart from the steric hinderance, those of ordinary skill in the art could not have believed that compounds P, Q, R, and S, administered to a subject as part of a pharmaceutical composition, would undergo the formation of cyclic imide to provide thalidomide. Consequently, Applicant respectfully requests that the rejection of claim 9 under 35 U.S.C. § 103(a) be withdrawn.

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[3] The Office Action indicates that the rejection of claims 9-12 over Billson, in view of Little, is maintained. Office Action, paragraph 22. However, Applicant notes that no previous rejection of claims 9-12 was made in the record. Applicant assumes that the rejection is directed to claim 9 only, based on the previous office action dated September 24, 2003.

D. Obviousness-Type Double Patenting

On pages 16-18 of the Office Action, the pending claims are provisionally rejected under judicially-created obviousness-type double patenting over certain claims of U.S. patent application nos. 09/480,448 and 10/430,892.[4] Since these rejections are provisional, Applicant respectfully requests that the rejections be held in abeyance until the claims are found otherwise allowable. Applicant will file a terminal disclaimer, if necessary, at such time.

No fee is believed due for the submission of this paper. If any fees are due for the submission of this paper, or to avoid abandonment of this application, please charge such fees to Jones Day Deposit Account No. 503013. A copy of this sheet is enclosed.

Respectfully Submitted,

Date: Feb. 22, 2005

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Enclosure

[4] The claims are also rejected over U.S. application no. 09/287,377 ("the '377 application"). However, the '377 application is this application. Thus, Applicant assumes that this rejection was mistakenly raised.